NDA 17-962/S-053 NOV 09 1999

Novartis Pharmaceuticals Corporation
Attention: Jerry Klimek
Associate Director, Drug Regulatory Affairs
59 Route 10
East Hanover, NJ 07936

Dear Mr. Klimek:

Please refer to your supplemental new drug application dated April 4, 1997, received April 10, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Parlodel (bromocriptine mesylate) Capsules/Tablets.

We acknowledge receipt of your submissions dated March 11, 1998 and August 13, 1998. Your submission of August 13, 1998 constituted a complete response to our April 3, 1998 action letter.

This supplemental new drug application provides for a new ***Pediatric Use*** subsection in the **PRECAUTIONS** section and a change in the **DOSAGE AND ADMINISTRATION** section to include pediatric dosage instructions as follows:

PRECAUTIONS section, ***Pediatric Use*** subsection:

"The safety and effectiveness of bromocriptine for the treatment of prolactin-secreting pituitary adenomas have been established in patients age 16 to adult. No data are available for bromocriptine use in pediatric patients under the age of 8 years. A single 8-year old patient treated with bromocriptine for a prolactin-secreting pituitary macroadenoma has been reported without therapeutic response.

The use of bromocriptine for the treatment of prolactin-secreting adenomas in pediatric patients in the age group 11 to under 16 years is supported by evidence from well-controlled trials in adults, with additional data in a limited number (n= 14) of children and adolescents 11 to 15 years of age with prolactin-secreting pituitary macro- and macroadenomas who have been treated with bromocriptine. Of the 14 reported patients, 9 had successful outcomes, 3 partial responses, and 2 failed to respond to bromocriptine treatment. Chronic hypopituitarism complicated macroadenoma treatment in 5 of the responders, both in patients receiving bromocriptine alone and in those who received bromocriptine in combination with surgical treatment and/or pituitary irradiation.

Safety and effectiveness of bromocriptine in pediatric patients have not been established for any other indication listed in the **INDICATONS AND USAGE** section."

DOSAGE AND ADMINISTRATION section, ***Hyperprolactinemia Indications*** subsection:

> "The initial dosage of Parlodel (bromocriptine mesylate) is ½ to 2 ½ mg SnapTabs® tablet daily. An additional 2 ½ mg SnapTabs® tablet may be added to the treatment regimen as tolerated every 2-7 days until an optimal therapeutic response is achieved. The therapeutic dosage is usually 5-7.5 mg and ranges from 2.5-15 mg daily.
>
> Based on limited data in children and adolescents 11 years of age and over (see ***Pediatric Use*** subsection) the initial dose is ½ to one 2 ½ mg tablet daily. The therapeutic dosage is usually 2.5-10 mg/day in divided doses in children and adolescents 11 years of age and older."

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text and with the minor editorial revisions listed below. Accordingly, the supplemental application is approved effective on the date of this letter.

Please revise the **DOSAGE AND ADMINISTRATION** section, ***Hyperprolactinemia Indications*** subsection to read:

> The initial dosage of Parlodel (bromocriptine mesylate) SnapTabs® in adults is one-half to one 2.5 mg scored tablet daily. An additional 2.5 mg tablet may be added to the treatment regimen as tolerated every 2-7 days until an optimal therapeutic response is achieved. The therapeutic dosage ranged from 2.5-15 mg daily in adults studied clinically.
>
> Based on limited data in children of age 11 to 15, (see ***Pediatric Use*** subsection) the initial dose is one-half to one 2.5 mg scored tablet daily. Dosing may need to be increased as tolerated until a therapeutic response is achieved. The therapeutic dosage ranged from 2.5-10 mg daily in children with prolactin-secreting pituitary adenomas.

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the submitted draft labeling text submitted August 13, 1998. These revisions are terms of the NDA Supplement approval.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 17-962/S-053." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MED WATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Jeanine Best, MSN, RN, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

Lisa D. Rarick, M.D.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research